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The Fission Yeast MCM-binding Protein, Mcb1, Regulates MCM Function during Pre-Replicative Complex Formation in DNA Replication

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The MCM complex is a replicative helicase, which is essential for chromosome DNA replication. In recent years, the identification of a novel MCM-binding protein (MCM-BP) in most eukaryotes has led to numerous studies investigating its function and its relationship to the MCM complex. However, the mechanisms by which MCM-BP functions and associates with MCM complexes are not well understood; in addition, the functional role of MCM-BP remains controversial and may vary between model organisms. The present study aims to elucidate the nature and biological function of the MCM-BP ortholog, Mcb1, in fission yeast. The Mcb1 protein continuously interacts with MCM proteins during the cell cycle *in vivo* and can interact with any individual MCM subunit *in vitro*. To understand the detailed characteristics of *mcb1*$^{+}$, two temperature-sensitive *mcb1* gene mutants (*mcb1*^{ts}) were isolated. Extensive genetic analysis showed that the *mcb1*^{ts} mutants were suppressed by a *mcm5*$^{+}$ multi-copy plasmid and displayed synthetic defects with many S-phase-related gene mutants. Moreover, CDK modulation by Cig2 repression or Rum1 overproduction suppressed the *mcb1*^{ts} mutants, suggesting the involvement of Mcb1 in pre-RC formation during DNA replication. These data are consistent with the observation that Mcm7 loading onto replication origins is reduced and S-phase progression is delayed in *mcb1*^{ts} mutants. Furthermore, the *mcb1*^{ts} mutation led to the redistribution of MCM subunits to the cytoplasm, and this redistribution was dependent on an active nuclear export system. These results strongly suggest that Mcb1 promotes efficient pre-RC formation during DNA replication by regulating the MCM complex.